



Film-shaped or wafer-shaped pharmaceutical preparation with masked taste

The invention relates to thin, film-shaped or wafer-shaped, orally applied active substance preparations for administration of active substances, preferably of pharmaceutical active substances. With these preparations, the active substances are preferably administered via the oral mucosa. Where the active substance preparations are swallowed, the active substances are released in the stomach and/or the intestine.

With conventional administration forms, e.g. tablets, which disintegrate and release the active substance in the stomach, the onset of action of the pharmaceutical product as a rule occurs only with a considerable delay in time. Although in the case of tablets that already disintegrate in the mouth and whose active substance is absorbed via the oral mucosa, this disadvantage is alleviated, it has to be taken into consideration that a considerable portion of the active substance preparation reaches the stomach with the saliva and is therefore not available for the quick absorption via the oral mucosa. In addition, following gastrointestinal absorption of the active substance the active substance is relatively quickly catabolized in the liver ("first pass effect").

For these and other reasons, thin administration forms, such as film-shaped or wafer-shaped preparations, for example, are of advantage. The, compared to the surface area, small thickness results in a short diffusion path when such a form of medicament is applied to the oral mucosa, for ex-

ample. This leads to a quick release of the active substance, which can be absorbed rapidly and directly through the oral mucosa.

Flat active substance carriers have already been developed and produced for various purposes. DE-OS 27 46 414, which describes a film-like web of active substance, binding agent and further auxiliary substances, can be regarded as fundamental for these administration forms. Due to the homogenous thickness, density and width of the web, there is a direct correlation between a unit of length of the web and the active substance dose contained therein. The advantages of continuous dosability have also been recognized by other applicants and described in special single variants. Thus, DE-PS 36 30 603 describes a flat-shaped carrier material, e.g. in the form of a release paper provided with an active substance-containing coating, the latter being strippable from the carrier material following previous separation into dosage units.

In DE-OS 196 52 188 there is described a flat pharmaceutical preparation which is suitable for application and release of the opiate analgesic buprenorphine in the oral cavity. With this administration form a mayor part of the amount of active substance contained therein is, however, transported via the saliva into the stomach and metabolised since the said administration form is not mucoadhesive or insufficiently mucoadhesive.

It is true that the general advantages of flat administration forms are known in the state of the art, e.g. a more rapid active substance release and easier dosability, which have already been mentioned, furthermore the possibility of taking the dosage form in a discreet manner, that is, without the aid of a liquid, furthermore advantages in manufac-

ture, and the possibility of printing on the administration form during the manufacture thereof, which results in increased safety in taking the medicine.

Despite the afore-described advantages such flat-shaped administration forms have so far been hardly successful. Presumably, many manufacturers of pharmaceuticals consider the advantage over conventional administration forms to be too small, so that it appears not to be profitable to develop products of this type and to obtain approval according to the law on pharmaceuticals. Especially where the active substance is orally applicable anyhow, there is a reluctance to accept the expenditure involved in the development of an alternative administration form, even if the advantages connected with this administration form are known.

A further reason why flat-shaped oral administration forms have hitherto hardly been successful is presumably insufficient patient compliance. Many active substances are characterized by a bitter taste so that oral administration thereof is accompanied by the sensation of an unpleasant taste, especially where the active agent is absorbed via the oral mucosa. This unpleasant taste sensation leads to a low acceptance of sheet-like oral administration forms with patients.

In the case of tablets and capsules which disintegrate and release the active substance in the stomach, the problems caused by the bitter taste of the active substances are as a rule solved by coating the administration form with a coating of neutral taste.

For thin, flat medicinal preparations which release the active substance in the oral cavity, coating of these administration forms with a coating of neutral taste is out of

the question. This approach to masking a taste is especially not possible with mucoadhesive and/or rapidly disintegrating flat administration forms where the active substance is to be released and absorbed by the oral mucosa as quickly as possible, or with administration forms which are applied as purely mucoadhesive systems over extended periods.

The object of the invention was therefore to provide thin, sheet-like pharmaceutical preparations for administration of active substances via the oral mucosa which no longer, or only to a strongly reduced degree, exhibit the disadvantages of a problematic taste sensation.

According to the invention, this object is achieved by film-shaped or wafer-shaped pharmaceutical preparations according to claim 1 and the preferred embodiments described in the subclaims.

The pharmaceutical preparations according to the invention are characterized by comprising a matrix which is formed of at least one matrix-forming polymer and which, apart from at least one active substance, also has at least one carbon dioxide-forming agent dissolved or dispersed therein.

The use of carbon dioxide-forming substances has already been described in connection with medicinal chewing gums. Thus, US patent 4,639,368 states that carbon dioxide-forming substances may be contained in the base material of the chewing gum preferably as fine granules having a size of less than 10  $\mu\text{m}$ .

Carbon dioxide-forming substances suitable for the pharmaceutical preparations according to the invention are pharmaceutically applicable monobasic to dibasic salts of car-

bonic acid, e.g. alkali metal hydrogen carbonates or alkali metal carbonates, alkali earth metal carbonates or ammonium carbonates and mixtures thereof, but other physiologically acceptable carbon dioxide-forming substances may also be utilized. Preferred carbon dioxide-releasing substances are sodium hydrogen carbonate, sodium carbonate, potassium hydrogen carbonate or potassium carbonate. Carbon dioxide-forming substances are known to those skilled in the art and may be effective when combined with each other.

To increase the development of  $\text{CO}_2$ , it is possible to add an acid component, e.g. sodium hydrogenphosphate or disodium hydrogenphosphate, sodium tartrate, sodium ascorbate or sodium citrate, as is usually the case in formulations for effervescent drinks. This enables the generation of carbon dioxide in a reaction between the acid and, for instance, a water-soluble bicarbonate salt as carbon dioxide-forming substance upon access of water after application of the medicinal oral preparation. Citric acid, tartaric acid, adipic acid, malic acid, ascorbic acid, succinic acid, acetic acid, fumaric acid, metatartaric acid, gluconic acid; lactic acid or phosphoric acid, for example, may be used as acids for the pharmaceutical preparations according to the invention. Especially preferred are organic acids which are suitable for human consumption. In addition, it can be of advantage to add acid regulators such as salts of acetic acid, for example.

Combined with an acid, but also without an acid, the sensation of taste in the case of oral application of a pharmaceutical preparation according to the present invention is, surprisingly, altered such that bitter-tasting substances or active agents do no longer produce this unpleasant sensation of taste, or do so only to a strongly reduced degree.

The pharmaceutical preparations according to the present invention are suitable for a plurality of different active substances.

It is, however, a precondition for a transmucosal, e.g. buccal or sublingual, application in the oral cavity that, taking into consideration the required dose, the oral mucosa is sufficiently permeable to the active substance. Permeability is, in turn, highly dependent on the physico-chemical properties of the active substance. In the case of pharmaceutical preparations according to the present invention which are to be swallowed it is a prerequisite that the active substances are absorbed in the stomach and/or the intestine.

Examples of active substances suitable for administration with the pharmaceutical preparation according to the invention are antipyretics and analgesics, e.g. ibuprofen, acetaminophen or aspirin; laxatives, e.g. phenolphthalein dioctyl sodium sulfosuccinate; appetite depressants, e.g. amphetamines, phenylpropanolamine, phenylpropanolamine hydrochloride or caffeine; antiacidics, e.g. calcium carbonate; antiasthmatics, e.g. theophylline; antidiuretics, e.g. diphenoxylate hydrochloride; agents active against flatulence, e.g. simethicon; migraine agents, e.g. ergotamine tartrate; psychopharmacological agents, e.g. haloperidol; spasmolytics or sedatives, e.g. phenobarbital (with or without atropine); antihyperkinetics, e.g. methyl dopa or methylphenidate; tranquilizers, e.g. benzodiazepines, hydroximeprobramate or phenothiazines; antihistaminics, e.g. astemizol, chlorpheniramine maleate; pyridamine maleate, doxylamine succinate, brompheniramine maleate, phenyltoloxamine citrate, chlorocyclizine hydrochloride, pheniramine maleate or phenindamine tartrate; deconges-

tants, e.g. phenylpropanolamine hydrochloride, phenylephrine hydrochloride, pseudoephedrine hydrochloride, pseudoephedrine sulfate, phenylpropanolamine bitartrate or ephedrine; beta-receptor blockers, e.g. propranolol; agents for alcohol withdrawal, e.g. disulfiram; antitussives, e.g. benzocaine, dextrometorphane, dextrometophane hydrobromide, noscapine, carbetapentane citrate or chlorthalidone hydrochloride; fluorine supplements, e.g. sodium fluoride; local antibiotics, e.g. tetracycline or cleocine; corticosteroid supplements, e.g. prednisone or prednisolone; agents against goiter formation, e.g. colchicine or allopurinol; antiepileptics, e.g. phenytoin sodium; agents against dehydration, e.g. electrolyte supplements; antiseptics, e.g. cetylpyridinium chloride; non-steroidal antiphlogistic active agents (antiphlogistics), e.g. acetaminophen, ibuprofen, dexiprofenlysinate, naproxen, or salts thereof; gastrointestinal active agents, e.g. loperamide or famotidine; various alkaloids, e.g. codeine phosphate, codeine sulfate or morphine; supplements for trace elements, e.g. sodium chloride, zinc chloride, calcium carbonate, magnesium oxide or other alkali metal salts and alkali earth metal salts; vitamins; ion-exchange resins, e.g. cholestyramine; cholesterol-depressant and lipid-lowering substances; antiarrhythmics, e.g. N-acetylprocainamide; or expectorants, e.g. guaifenesin.

To be mentioned in particular are the following active agents: ketoprofen, ibuprofen, loperamide, selegiline, antipamezol, nicotine, quinine, bruzine, paracetamol, dextrometorphane, caffeine and other xanthines such as theophyllines and theobromines, pyrazolones such as metamizol, magnesium sulfate, zopiclone or zolpidem.

Furthermore, pharmacologically active substances are also suitable as active agents; these are contained in the following classes or groups:

$\alpha$ -adrenergic agonists;  $\beta$ -adrenergic agonists;  $\alpha$ -adrenergic blockers;  $\beta$ -adrenergic blockers; alcohol withdrawal agents; aldose-reductase inhibitors; anabolics; narcotic analgesics, preferably codeine, morphine derivatives; non-narcotic analgesics, preferably salicylates and their derivatives; androgens; anaesthetics; appetite depressants; anthelmintics (active against cestodes, nematodes, Onchocerca, schistosomes or trematodes); anti-acne agents; anti-allergics, anti-amoebic agents (amoebicidal agents); anti-androgens; agents against angina pectoris; antiarrhythmics; anti-arteriosclerotic agents; anti-arthritic/antirheumatic agents; antibacterial agents (antibiotics), preferably aminoglycosides, amphenicols, ansamycines,  $\beta$ -lactams (especially carbapenemes, cephalosporins, cephamycines, monolactams, oxacephemes, penicillins), lincosamides, macrolides, polypeptides, tetracyclines; synthetic antibacterial agents, preferably 2,4-diaminopyrimidines, nitrofurans, quinolones and quinolone analogues, sulfonamides, sulfones; anticholinergics; anticonvulsants; antidepressants, preferably bicyclic antidepressants, hydrazides, hydrazines, pyrrolidones, tetracyclic antidepressants; tricyclic antidepressants, polycyclic imides; antidiabetic agents, preferably biguanides, sulfonyl-urea derivatives; antidiarrhoeal agents; antidiuretics; anti-estrogens; antimycotics/fungicidal agents, preferably polyenes; synthetic antimycotics/fungicidal agents, preferably allylamines, imidazoles, triazoles; antiglaucoma agents; antigonadotropins; agents against gout; antihistaminics, preferably alkylamine derivatives, aminoalkyl ethers, ethylenediamine derivatives, piperazines, tricyclic compounds (especially phenothiazines); antihyperlipoproteinaemic agents (lipid-

lowering agents), preferably aryloxyalcanoic acid derivatives (especially clofibrinic acid derivatives and analogues), bile acid-sequestering (masking) substances, HMG-CoA-reductase inhibitors, nicotinic acid derivatives, thyroid gland hormones and analogues thereof; anti-hypertensive/blood pressure-lowering agents, preferably benzothiadiazine derivatives, N-carboxyalkyl-(peptide/lactam) derivatives, guanidine derivatives, hydrazines/phthalazines, imidazole derivatives, quaternary ammonium compounds, quinazoline derivatives, reserpine derivatives, sulphonamide derivatives; agents against hyperthyroidism; agents against hypotension; agents against hypothyrosis; non-steroidal anti-inflammatory agents (antiphlogistics), preferably aminoarylcarboxylic acid derivatives, arylacetic acid derivatives, arylbutyric acid derivatives, arylcarboxylic acid derivatives, arylpropionic acid derivatives, pyrazoles, pyrazolones, salicylic acid derivatives, thiazine carboxamide; antimalarial agents, preferably quinine and its salts, acids and derivatives; anti-migraine agents; agents against nausea; antineoplastic agents, preferably alkylating agents (especially alkyl sulfonates, aziridines, ethyleneimines and methylmelamines, nitrogen mustard gases, nitrosoureas), antibiotic agents, antimetabolites (especially folic acid analogues, purine analogues, pyrimidine analogues), enzymes, interferons, interleukins; hormonal antineoplastic agents, preferably androgens, anti-adrenal agents, anti-androgens, anti-estrogens (especially aromatase inhibitors); antineoplastic dietary additives; anti-Parkinson agents; agents against pheochromocytomae; agents against pneumocystis; agents for treating hypertrophy of the prostate; protozoacide agents, preferably against Leishmania, Trichomonas, Trypanosoma; antipruritic agents; antipsoriatic agents; antipsychotic agents, preferably butyrophenones, phenothiazines, thioxanthenes, other tricyclic agents, 4-arylpiperazine, 4-arylpiperidine; antipyretic agents; agents against rickettsiae; agents against

seborrhoea; antiseptics, preferably guanidine, halogens and halogen compounds, nitrofuranes, phenols, quinolines; antispasmodic/spasmolytic agents; antithrombotics; antitussives; anti-ulcus agents; uricostatics (antiurolithics); antivenenum; antiviral agents, preferably purines, pyrimidinones; anxiolytics, preferably arylpiperazines, benzodiazepine derivatives, carbamates; benzodiazepine antagonists; bronchodilators, preferably ephedrine derivatives, quaternary ammonium compounds, xanthine derivatives; calcium channel blockers, preferably arylalkylamines, dihydropyridine derivatives, piperazine derivatives; calcium regulators; cardiotonics; chelate or complex formers; cholecystokinin antagonists; cholelitholytic agents; choleretics; cholinergics; cholinesterase inhibitors; cholinesterase reactivators; CNS stimulants; decongestion agents; prophylactic agents against dental caries; depigmenting agents; diuretics, preferably organic mercury compounds, pteridines, purines, steroids, sulphonamide derivatives, uracils; dopamine receptor agonists; agents against ectoparasites; enzymes, preferably digestive enzymes, penicillin-inactivating enzymes, proteolytic enzymes; enzyme-inducing agents; steroidal and non-steroidal estrogens; gastric secretion inhibitors; glucocorticoids; gonad-stimulating active agents; gonadotropic hormones; growth hormone inhibitors; growth hormone-releasing factor; growth stimulants; haemolytic agents; heparin antagonists; hepatoprotective agents, agents for treating diseases of the liver; immunomodulators; immunosuppressing agents; ion exchange resins; lactation-stimulating hormones; LH-RH agonists; lipotropic agents; agents against lupus erythematosus; mineralocorticoids; miotics; monoaminoxidase inhibitors; mucolytics; muscle relaxants; narcotics antagonists; neuroprotective agents; nootropics; ophthalmics; ovarian hormones; oxytocics; pepsin-inhibitors; peristaltic stimulants; progestogens; prolactin inhibitors; prostaglandins and prostaglandin analogues; protease inhibitors; respira-

tory stimulants; sclerosing agents; sedatives/hypnotics, preferably acyclic ureides, alcohols, amides, barbituric acid derivatives, benzodiazepine derivatives, bromides, carbamates, chloral derivatives, piperidinediones, quinalone derivatives; thrombolytics; thyreotropic hormones; uricosurics; vasodilators (cerebral); vasodilators (coronary); vasodilators (peripheral); vasoprotective agents; vitamins, vitamin precursors, vitamin extracts, vitamin derivatives; vulneraries.

Active substances which have a particularly unpleasant taste are antibacterial agents based on pyridonecarboxylic acid, with 5-amino-1-cyclopropyl-6,8-difluoro-7-(cis-3,5-dimethyl-1-piperazinyl)-1,4-dihydro-4-oxoquinolone-3-carboxylic acid being regarded as particularly unpleasant, enoxacine, pipemdic acid, ciprofloxacin, ofloxacin and pefloxacin, antiepileptics such as zonisamide, macrolide antibiotics such as erythromycin, beta-lactam antibiotics such as penicillins or cephalosporins, psychotropic active substances such as chlorpromazine, active substances such as sulpyrine, or agents active against ulcers, such as cimetidine.

The above list of active substances that according to the present invention can be administered with the administration form is not complete. The present invention also encompasses preparations containing a combination of one or more active substances. Such a preparation can be of advantage in various respects since it is possible to incorporate any therapeutically useful active agent in the preparation according to the invention.

This means that several concomitant symptoms or conditions can be treated by means of a fixed active substance combination in a single medicament.

To support the active substance uptake via the oral mucosa, a preferred embodiment provides for the addition of agents which accelerate the uptake of active agent (permeation enhancers). Suitable permeation enhancers are, in particular: propanediol, dexpanthenol, oleic acid; the enhancer(s) may, for example, be selected from the following group: saturated or unsaturated fatty acids, hydrocarbons, straight-chain or branched fatty alcohols, dimethyl sulfoxide, propylene glycol, decanol, dodecanol, 2-octyldodecanol, glycerol, isopropylidene glycerol, transcitol (= diethyleneglycol-monoethyl ether), DEET (= N,N-diethyl-m-tolueneamide), solketal, ethanol or other alcohols, menthol and other essential oils or components of essential oils, lauric acid diethanolamide, D-alpha-tocopherol and dexpanthenol; the above list is not complete.

Combinations of two or more enhancer substances can also be used to advantage.

The uptake of active substance can furthermore be improved by means of substances stimulating the blood flow which can be added to the preparations according to the invention. Among these are, in particular: menthol, eucalyptol, ginkgo extract, geranium oil, camphor, spearmint oil, oil of juniper and rosemary. These blood flow-stimulating substances may be used singly or in combination with one or more of the afore-mentioned permeation-enhancing substances.

According to a particular embodiment, the inventive film-shaped or wafer-shaped pharmaceutical preparations are capable of disintegrating. They can be configured, for example, as quickly disintegrating administration forms, i.e. administration forms disintegrating within a period of 1 second up to 3 minutes, or as slowly disintegrating administration forms, i.e. administration forms disintegrating within a period of 3 to 15 minutes. But administration

forms which can be sucked also represent a subject matter of the present invention.

Systems which are mucoadhesive but do not disintegrate or erode, or do so very slowly, must be removed after the active substance has been released; the retention time of these systems can be up to several hours.

The disintegration process should substantially be completed within 15 min if the medicament form adhering to the oral mucosa was surrounded during this period by an aqueous medium, e.g. a body fluid. According to preferred embodiments of the invention, the pharmaceutical forms are configured such that they disintegrate within 3 min, and with particular preference within 60 s, after introduction in an aqueous medium.

The disintegration times indicated are based on the measurement of disintegration times according to Pharm. Eur. 2.9.1 "Zerfallszeiten von Tabletten und Kapseln" [Disintegration Times of Tablets and Capsules].

The indicated disintegration times can be set to the above-mentioned ranges by using matrix-forming polymers which have different disintegrating, respectively solubility characteristics. A pharmaceutical preparation based on polyvinyl alcohol, for example, will disintegrate much more quickly than a medicinal HPMC preparation. Thus, by mixing the corresponding polymer components, the disintegration time can be adjusted. In addition, disintegrants are known which "draw" water into the matrix and cause the matrix to burst open from within. As a consequence, it is also possible to add such disintegrants for the purpose of adjusting the disintegration time.

The matrix of the inventive, quickly disintegrating administration forms contains as base materials a water-soluble polymer, or mixtures of such polymers. Synthetic or par-

tially synthetic polymers or biopolymers of natural origin which are film-forming and water-soluble are used with preference for this purpose. Especially suitable are polymers which are preferably selected from the group comprising cellulose derivatives, polyvinyl alcohol (e.g. Mowiol®), polyacrylates and polyvinyl pyrrolidone.

Of the cellulose derivatives hydroxypropylmethyl cellulose, carboxymethyl cellulose, sodium-carboxymethyl cellulose (e.g. Walocel), hydroxyethyl cellulose, hydroxypropyl cellulose and methyl cellulose are particularly preferred. Also preferred are water-soluble polysaccharides of plant or microbial origin, especially pullulan, xanthan, alginates, dextrans and pectins. Furthermore, proteins, preferably gelatine or other gel-forming proteins are suitable. In addition, starch and starch derivatives; gelatine (various types); polyvinyl pyrrolidone; gum arabic; pullulan; acrylates; polyethylene oxide, especially the Polyox 10, Polyox 80, Polyox 205, Polyox 301, Polyox 750 types (Union Carbide); copolymers of methylvinyl ether and maleic acid anhydride (Gantrez-Copolymers, especially the ES, MS and S types; ISP Global Technologies GmbH).

For the structure of a matrix which releases the active substance slowly, the polymers used with preference are those selected from the group comprising cellulose ethers, preferably ethyl cellulose, as well as polyvinyl alcohol, polyurethane, polymethacrylates, polymethyl methacrylates and derivatives and copolymerisates of the aforementioned polymers.

The polymer film's poor solubility or insolubility in aqueous medium, or its water-resistant configuration, results in the active substance release taking place only slowly by way of diffusion and - given a suitable formulation - with

a slow diffusion coefficient. This leads to a slow release of active substance.

To reduce the solubility, respectively the release rate, of the slow-release layer(s), the polymer layer may be subjected to annealing. Thus, a highly hydrolysed polyvinyl alcohol, for example, may be used as a base polymer for the insoluble, slow-releasing layer if said alcohol is rendered insoluble by annealing.

With the preparations according to the present invention, the active substance release takes place by way of permeation through the oral mucosa. As a prerequisite for this, the flat preparation must be in close contact with the mucosa during the period of application, i.e. if possible until the dissolution or disintegration of the preparation has taken place. By choosing suitable auxiliary substances, it is possible to produce improved contact between the inventive pharmaceutical preparation and the oral mucosa. For this reason, the pharmaceutical preparation according to a preferred embodiment of the invention contains an adhesion-imparting auxiliary substance or auxiliary substance mixture imparting bio-adhesive or mucoadhesive properties to the preparation. Certain orally applicable auxiliary substances which are usual in pharmaceuticals are known to possess mucoadhesive properties. Examples for such mucoadhesive substances are polyacrylic acid, carboxymethyl cellulose, hydroxymethyl cellulose, methyl cellulose, tragacanth, alginic acid, gelatine and gum arabic. Furthermore, various non-mucoadhesive substances are known also to develop mucoadhesive properties in certain mixing ratios. An example for such a mixture is glycerol mono-oleate/water with a ratio of 84:16 (Engström et al., Pharm. Tech. Eur. 7 [1995], No. 2, p. 14-17).

When using bio-adhesive or mucoadhesive auxiliary substances, a bilayer or multilayer structure of the administration form of the inventive preparation is to be preferred. Because of the fact that only the layer or layers which is/are facing, respectively are in contact with, the oral mucosa is/are rendered mucoadhesive, but not the distal or outwardly located layer or layers, it is possible to avoid that the preparation, during the period of application, causes different parts of the mucosa to stick together, which would lead to considerable unpleasant sensations in use. Preferred embodiments are therefore bilayer or multilayer, with one of the two layers, or in the case of a multilayer structure one of the layers, having mucoadhesive properties. This structure is preferred for non-disintegrating or only very slowly disintegrating or eroding systems.

In the case of embodiments which apart from mucoadhesive layers also contain non-mucoadhesive layers, the latter are preferably configured such that their permeability for the active substance is lower than that of the bio-adhesive or mucoadhesive layer. In this way, the active substance can be prevented from being released into the saliva of the oral cavity, which would lead to loss of active substance.

The mentioned pharmaceutical preparations are comparatively dense structures preferably having a density between 0.3 g/cm<sup>3</sup> and 1.7 g/cm<sup>3</sup>, especially preferably between 0.5 g/cm<sup>3</sup> and 1.5 g/cm<sup>3</sup>, and most preferably between 0.7 g/cm<sup>3</sup> and 1.3 g/cm<sup>3</sup>.

The total thickness of the preparations according to the invention is preferably 5 µm up to 10 mm, preferably 30 µm to 2 mm, and with particular preference 0.1 mm to 1 mm. The pharmaceutical preparations may advantageously be of round,

oval, elliptic, triangular, quadrangular or polygonal shape, but they may also have any rounded shape.

The surface of the preparations according to the invention is usually smooth; it may, however, be of advantage to provide the surface with elevations and deepenings, e.g. in the form of knobs or grooves.

The invention also includes preparations of the kind mentioned herein which are present in the form of thin, solid foams. Wafers in the form of thin foams are advantageous since they quickly adhere to the mucosa due to their large specific surface, and since they on the other hand also disintegrate quickly. The density of these solidified foams is preferably between  $0.01 \text{ g/cm}^3$  and  $0.8 \text{ g/cm}^3$ , with particular preference between  $0.08 \text{ g/cm}^3$  and  $0.4 \text{ g/cm}^3$ , and with greatest preference between  $0.1 \text{ g/cm}^3$  and  $0.3 \text{ g/cm}^3$ . When calculating the density, the volume filled or enclosed by the entire foam body is taken as the basis for calculation.

The above-mentioned foams may be produced by introducing and dispersing gases with the aid of special foam beating devices, or by dissolving gas under pressure and subsequent relaxation of the solution.

The matrix of the inventive medicinal preparations has at least one matrix-forming polymer. The matrix-forming polymer(s) constitute(s) a substantial component of the matrix; the polymer portion amounts to at least 3%-wt. and maximally 98%-wt., preferably 7 to 80%-wt., with particular preference 20 to 50%-wt., each value being relative to the entire preparation. The mucoadhesive properties as well as the disintegration properties are determined substantially by the type of the matrix-forming polymer(s), as well as by the relative proportions of these polymers in the preparation.

To further reduce the adhesion tendency of the administration forms, it is also possible for the surfaces of the administration form to be of uneven or irregular shape, preferably undulatory or relief-like. Such an irregular surface structure may be caused, for example, by the bubble-shaped cavities which are introduced in the polymer matrix.

Apart from the matrix-forming polymers, auxiliaries may optionally be added to the matrix. For this purpose the following are taken into consideration: fillers (e.g.  $\text{SiO}_2$ ); dyes and pigments (e.g. quinoline yellow or  $\text{TiO}_2$ ); disintegrants, especially disintegrants which draw water into the matrix and which burst the matrix from within (e.g. aerosil); emulsifiers (e.g. polyethoxylated sorbitan fatty acid esters such as TWEEN<sup>®</sup> or polyethoxylated fatty alcohols such as BRIJ<sup>®</sup>); plasticizers (e.g. polyethylene glycol, glycerol); sweeteners (e.g. aspartame, saccharin); preserving agents (e.g. sorbic acid and its salts), and flavouring agents.

Furthermore, stabilisers or antioxidants may also be added as auxiliaries, such as, for example, ascorbyl palmitate, sodium disulfite, vitamin E, vitamin A, vitamin C; both singly and in combination with each other, or in combination with other auxiliaries.

According to a preferred embodiment, the preparations according to the invention contain at least one flavouring substance and/or at least one sweetener and/or at least one plasticizer.

The composition of the preparations according to the invention will be illustrated by way of example with reference

to the following recipes, without thereby limiting the scope of the invention:

Example:

	Example 1	Example 2
Metolose 60 SH 50	45,0	45,0
Aspartame	10,0	10,0
Mannitol	10,0	10,0
Menthol	5,0	5,0
Flavouring	10,0	5,0
Titanium dioxide	-	5,0
Sodium hydrogencarbonate	10,0	10,0
Loperamide	10,0	10,0

In a taste testing it was shown that addition of 10%-wt of sodium hydrogencarbonate, corresponding to 2.0 mg/wafer, leads to the complete disappearance of the sensation of the bitter taste of loperamide.